



PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Applicants:** Craig Myers, et al.

**Examiner:** L. Wong

**Serial No.:** 09/666,369

**Art Unit:** 1761

**Filing Date:** September 20, 2000

**Docket:** 13028

05 -02- 2004

**For:** ANHYDROUS LACTITOL CRYSTALS, A  
PRODUCT CONTAINING THE SAME AND A  
PROCESS FOR THE PREPARATION THEREOF  
AS WELL AS USE THEREOF

Commissioner for Patents  
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 C.F.R. §1.132**

I, Juha Nurmi, declare and state as follows:

1. I am one of the inventors of the above-identified application, and I have complete knowledge of all aspects of the invention embodied therein.
2. I received a Master's degree in Chemical Engineering in October 1984 from the Helsinki University of Technology. I am currently studying towards a Doctorate or Licentiate at the Lappeenranta University of Technology. From my research, to date, I have authored seven peer-reviewed publications and have obtained several patents. A listing of my publications is attached hereto as Exhibit A.
3. I have been employed by Danisco Sugar Oy (former Cultor Oy) as a researcher in Danisco Sugar & Sweeteners Development Center since 1985. The assignee of the above-identified application is a subsidiary of Danisco. I was hired as a carbohydrate crystallization

chemist; in 1993, I was promoted to group leader of a crystallization research group, which consists of several scientists and technicians.

4. I have been quite active in the field of saccharide chemistry since 1985 and have spent many years investigating the chemistry of the various forms of lactitol.

5. In connection with U.S. Patent application serial no. 09/666,369, I have been asked to compare the invention described and claimed in the above-identified application with the subject matter described in WO 92/16542, in which Heikkila, et al. are listed as inventors (hereinafter "WO 92/16542" or "Heikkila, et al.").

6. I have read and am quite conversant with the teachings in WO 92/16542.

7. The present invention is directed to a new crystal form of lactitol, viz.,  $\beta$ -lactitol, namely anhydrous  $\beta$ -lactitol, and to the process of making the same and the uses thereof.

8. WO 92/16542 is directed to anhydrous  $\alpha$  lactitol. Its teachings are limited to  $\alpha$ -lactitol and its use. Its teachings are limited to  $\alpha$ -lactitol. There is no discussion therein of  $\beta$ -lactitol, the subject matter of the present invention.

9. There are many differences between  $\beta$ -lactitol of the present invention and the  $\alpha$ -lactitol. Quite noticeably the crystal structures are different. The crystal structure of the  $\beta$  lactitol is orthorhombic, which is totally different from that of the prior art monoclinic  $\alpha$  lactitol crystals described in WO 92/16542.

10. Moreover, the x-ray diffraction pattern of  $\beta$ -lactitol is quite different from that of the  $\alpha$ -lactitol indicating that the  $\alpha$ -form described in WO 92/16542 and the  $\beta$  form described in the above-identified application are quite different. The space group for the orthorhombic  $\beta$ -lactitol is P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, in contrast to the monoclinic  $\alpha$ -lactitol, which is P2<sub>1</sub>. The  $\beta$ -lactitol produced in accordance with the present invention has unit cell parameters of about a =



9.6 Å, b = 11.1 Å, c = 14.0 Å and V = 1502 Å<sup>3</sup>. On the other hand, the anhydrous  $\alpha$  lactitol crystals produced in accordance with the procedure described in WO 92/16542 had quite different unit cell parameters, a = 7.614 Å, b = 10.757 Å, c = 9.370 Å and V = 729 Å<sup>3</sup>, as described on Page 4, lines 3-7 thereof, further evidencing that the  $\beta$ -lactitol is quite different from the  $\alpha$ -lactitol.

11. Moreover, when the process described in Heikkila, et al. was repeated it was found to produce  $\alpha$ -lactitol and only  $\alpha$ -lactitol; x-ray diffraction is a very sensitive technique, and if any  $\beta$ -lactitol were formed, it would have detected same. Yet, when the product of the process described in the Heikkila, et al. was subjected to x-ray diffraction, the x-ray diffraction pattern revealed no  $\beta$ -lactitol formation. Further, there is no indication of the presence of any  $\beta$ -lactitol in the process described in the Heikkila, et al. reference, and no  $\beta$ -lactitol has ever been alleged to be produced in WO 92/16542.

12. In addition, the x-ray diffraction pattern of the  $\beta$ -lactitol was different from that of other lactitols known, such as lactitol monohydrate. The x-ray diffraction pattern did not fit anhydrous lactitol obtained by drying lactitol monohydrate. Moreover, the x-ray diffraction pattern did not correspond to a mixture of both anhydrous  $\alpha$ -lactitol and monohydrate. In short, the X-ray diffraction pattern of the  $\beta$ -lactitol of the present invention does not correspond to the various lactitols of which I was aware. Since the x-ray diffraction pattern was different from other known lactitols, the only conclusion that can be drawn is that the  $\beta$ -lactitol is different from the other known lactitols.

13. Moreover, samples of old commercial lactitols and  $\alpha$ -lactitol samples as well as laboratory produced  $\alpha$ -lactitol samples present in my laboratory were systematically tested to



check whether any  $\beta$ -lactitol were present in any of them. Not a single sample of  $\alpha$ -lactitol has been found to contain even traces of  $\beta$ -lactitol.

14. The present inventors have found that  $\alpha$ -lactitol crystals would transform with time into the  $\beta$ -lactitol form only in the wet state, provided that crystallized  $\alpha$ -crystals were retained in the mother liquor at a constant temperature between 100 and 70°C. The amount of time for complete transformation varied with temperature and took from several hours to several days. Since the process in WO 92/16542 did not teach or suggest maintaining a crystal mass in the mother liquor for any prolonged time at an elevated temperature, I further conclude that no  $\beta$ -lactitol was formed in the process described therein.

15. Other methods for making the  $\beta$ -lactitol forms were also not described or suggested in WO 92/16542. For example, the present inventors found that a wet transformation from  $\alpha$ -lactitol into  $\beta$ -lactitol occurred when the crystallization procedure was very slow. This meant that the supersaturation of the solution in  $\alpha$ -lactitol was very close to zero and the crystals were formed very slowly and remained in solution for a prolonged period of time. This process also was not described or discussed or suggested in WO 92/16542.

16. Once the pure  $\beta$ -lactitol crystals are produced, they could be used as seed crystals in the boiling or cooling crystallization process described in the above-identified application. With such  $\beta$  seeding, the crystal mass would be formed in the  $\beta$ -form. This seeding process using  $\beta$ -lactitol crystals was not taught, disclosed or suggested in WO 92/16542.

17. The unique crystal structure of the  $\beta$ -lactitol manifests itself in properties which are not only different but which are unexpected relative to those of the  $\alpha$ -lactitol described in WO 92/16542. Because the crystal structures are different, the crystal related properties of the  $\alpha$ -lactitol and  $\beta$ -lactitol are quite different.



18. This difference in crystal structure gives the  $\beta$ -crystal form unexpected advantages relative to the  $\alpha$  form. Some of these advantages are described on Page 8 of the above-identified application. For example, the  $\beta$ -lactitol exhibits improved shelf life because of the lower hygroscopicity. In addition, compositions of matter containing the  $\beta$ -lactitol have enhanced mouth feel (because of the greater hardness and higher heat of fusion).  $\beta$ -lactitol crystals are very stable and they are harder than the  $\alpha$ -lactitol crystals. This gives technical advantages, e.g., in special chocolates. The  $\beta$ -lactitol has a lower solubility at high temperatures than the  $\alpha$ -lactitol. This affects the way the two lactitol forms dissolve in liquids during use and processing. The melting enthalpy of the  $\beta$  lactitol is higher than that of the  $\alpha$ -lactitol, which means that it needs more heat to melt or, contrarily, it keeps solid for a longer time without melting.

19. The differences between the two anhydrous lactitol forms are more marked at high temperatures and in moist conditions. These differences result in significantly improved foods, confectionary and toothpastes produced from  $\beta$ -lactitol as compared to similar products produced from  $\alpha$ -lactitol. Although the  $\beta$ -lactiol may substitute for the  $\alpha$  lactitol in most applications, the improved stability of the  $\beta$ -lactitol exhibits a technical advantage. In my opinion, the technical merits of the  $\beta$ -lactitol crystals open up new markets and provide new applications for the  $\beta$ -lactitol.

20. It is evident that  $\beta$ -lactitol has properties different from those of the  $\alpha$ -lactitol crystals produced in WO 92/16542. These different properties are unexpectedly advantageous and have an influence on the technical utility and industrial applicability of the  $\beta$ -lactitol form.

21. Thus, in my opinion the teachings of WO 92/16542 are limited to  $\alpha$ -lactitol and the method of using same. The  $\beta$ -lactitol of the present invention, the methods of preparing



same and the method of using the same in preparing various compositions of matter as well as the compositions of matter so prepared are not taught, described or suggested in WO 92/16542. Moreover, the  $\beta$ -lactitols have unexpected properties relative to the  $\alpha$ -lactitol described in WO 92/16542.

22. It is my opinion that the present invention represents a significant advancement in the art.

23. The undersigned discloses further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 25th February, 2004



Juha Nurmi